The First NIAID Workshop in Medical Mycology:

Molecular Medical Mycology
University of Minnesota
Minneapolis, MN
June 24-26, 1993

PREFACE

The NIAID recognizes medical mycology as an area in need of development. An Institute sponsored workshop on "Mycology Research in the 1990's" in Chicago, Illinois, 28-29 September 1991 addressed the increasing importance of medical mycology. Twenty medical mycologists from throughout the United States were invited to the discuss the issues and to conceptualize and condense the active research areas into topic areas in need of development.

Five areas were targeted for focus. These were: molecular mycology, diagnosis and treatment, immunology, antigen structure and function, and epidemiology. Each of these five topic areas was targeted for development into a separate workshop/minisymposium, co-sponsored by the NIAID and educational grants raised by the medical mycological community.

"Molecular Medical Mycology," the first workshop in the series, was held in Minneapolis, MN on 24-26 June, 1993. One hundred and forty-seven mycologists attended and exchanged ideas. A key to the success of information exchange was the utilization of "break out" sessions that provided an informal setting for free exchange of ideas, an opportunity for a more active involvement for all of the participants, and an environment fostering new collaborations.

I believe the workshop series is off to an auspicious start, and that this success is representative of the field of medical mycology whose time has come. Finally, I would like to thank all those who contributed to the success of this workshop, including all of the participants, organizing and writing committees, and especially Dr. Paul T. Magee whose far reaching vision and role as workshop Chair have helped to set the stage for future endeavors of this kind.

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INTRODUCTION

The workshop was designed to present an overview of the biological systems represented by fungal pathogens of man and to encourage innovative approaches directed at the public health problems posed by the fungi. Each of five topic sessions was organized around a theme presentation giving a general overview of a medically important fungus and was followed by research presentations giving specific advances in related, non-medical model systems. Each of the five topic sessions was followed by one hour "break out" sessions of 10 to 15 participants led in discussion by group facilitators who subsequently summarized the results in separate "at large" discussions.

The mycological community responded to NIH interest by their presence and participation in the workshop. There was balanced representation from the medical and non-medical mycological groups including clinical and laboratory based medical mycologists, industrial mycologists, fungal geneticists, plant pathologists, and model systems mycologists.

Indications are that the field of molecular medical mycology is ready to "take off." As evidenced in the theme presentations, there is an outstanding body of descriptive work on fungal diseases and the causal organisms. Many of the problems appear to be clearly defined, making it possible to formulate specific, reasonable hypotheses about mechanisms underlying the disease process. This wealth of information, however, is not highly accessible to many of the scientists who are equipped to put these hypotheses to the test. By contrast, the research presentations demonstrated how much can be done with model systems.

The research tools provided by model systems using *Saccharomyces cerevisiae*, *S. pombe*, and *Aspergillus nidulans* have permitted detailed elucidation of regulatory pathways. Clear relational themes emerged of direct relevance to medical mycology. For example, the pathways controlling dimorphism in *S. cerevisiae* and sporulation in *A. nidulans* are related and it seems very likely these are in turn related to analogous (homologous?) pathways in pathogenic fungi, for example *Candida albicans*. All the tools are available to determine if this is true and, if so, to interface the medical systems with the appropriate model systems.

Key Concepts emerging from the workshop are listed below. Individual topics are summarized in the following pages.

- The field of medical mycology is ready to "take off"
- Development of genetic systems will be a key to advancing the field
- Fungal virulence remains largely unexplained
- The relevance of the mycoses is under-appreciated
- Mycological communications and interactions could be improved

MORPHOGENESIS

Current Status

Morphogenesis flexibility is a hallmark of the pathogenic fungi. Many fungal pathogens of animals, in particular those that cause subcutaneous and deep mycoses, are characterized by varying degrees of "morphogenetic plasticity" both *in vitro* and *in vivo*. This feature is well illustrated by the causative agents of candidiasis, chromoblastomycosis, mucormycosis, entomophthoramycosis and phaeohyphomycosis, and was the principal theme of this session. The cell wall ultimately determines fungal morphology. Plasticity of the growing cell has yielded the multiplicity of forms observed amongst the parasitic fungi. The respiratory fungal pathogens most frequently encountered by clinicians demonstrate several common morphogenetic features. The airborne conidium of these fungi is usually the infectious agent. The survival of conidia in the lungs and their ability to differentiate into tissue-borne parasitic cells are pivotal for successful infection of the host. Morphological changes and molecular events which accompany the transition of conidium to parasitic cell (yeast, hypha, spherule) merit our careful examination.

Coccidioides immitis, the causative agent of a respiratory disease known as "valley fever," has one of the most interesting morphogenetic cycles and was used to illustrate certain common molecular features of parasitic fungal development. Cell wall growth and differentiation were the focus of attention. Concomitant events of wall synthesis and hydrolysis occur during early transformation of the conidium to parasitic cell. High levels of chitin synthesis occur within the spherule of *C. immitis* during the segmentation process.

Spherule segmentation is followed by differentiation of endospores within the still-intact spherule envelope. Ultimately, the function of molecules suspected to perform key roles in fungal growth and development must be evaluated by recombinant DNA technology. The identification and characterization of novel molecular targets for inhibition of fungal morphogenesis are at hand.

Success in such efforts will most likely be achieved by the cooperation of investigators whose focus as a group spans the range from the whole organism and its morphogenesis to the gene, its expression, and its mechanisms of regulation.

Valuable information on morphogenetic cycles which is relevant to research problems in medical mycology is not confined to pathogenic fungi. *Saccharomyces cerevisiae* has long been known to undergo pseudohyphal growth, and a genetic and molecular analysis of this phenomenon is well underway. As genes regulating pseudohyphal growth are identified in *S. cerevisiae*, their homologues in *Candida albicans*, *Histoplasma capsulatum*, and other pathogens will be more easily identified and may serve as novel drug targets. Similarly, the detailed knowledge of the pathway of conidiation in *Aspergillus nidulans* may lend to interventions not only in diseases caused by pathogens of this genus but in other diseases whose causative agents infect via conidia. A particular morphogenetic switch in *C.. albicans* is being analyzed at the molecular level and several apparently form-specific genes have been identified. These may give insight into the mechanism of regulation of the morphogenetic change. Since there is evidence that this cycle is involved in pathogenesis, such insight could be important in designing anti-*Candida* drug therapy.

Recommendations

- As we identify specific molecules which are involved in morphogenesis, strong efforts should be made to isolate the corresponding genes, since these genes can tell us much about the structure and function of the molecules.

- As model systems like *Saccharomyces* and *Aspergillus* yield increasing information about morphogenesis, research cooperation between investigators studying those systems and medical mycologists should be intensified. We cannot afford to spend time and effort reinventing the wheel, and medically important systems are intrinsically much harder to work with in the laboratory.

Efforts should be directed into building the scientific infrastructure (libraries, maps, transformation systems and vectors) in organisms of medical importance which do not have an obvious model system counterpart (*Coccidioides* is an excellent example).

SEXUAL AND ASEXUAL CYCLES

Current Status

Our understanding of fungal pathogenicity at the molecular level cannot begin without a knowledge of the life cycle of a given pathogen. This is because pathogenicity is often associated with certain morphological forms or a certain part of the life cycle of a fungal species. For example, dimorphic pathogens such as *Histoplasma capsulatum*, *Coccidioides immitis* or *Sporothrix shenckii* convert from one morphological form to another in the host tissue before they propagate to cause disease. *Cryptococcus neoformans* causes infection only in the asexual form of its life cycle (yeast cells).

The fungi which have been used as model systems for molecular study are mostly Ascomycetes (such as *Neurospora crassa, Apergillus nidulans, Saccharomyces cerevisiae* and *Schizosaccharomyces pombe*) and are rarely or never pathogenic. The research tools provided by these species have contributed to substantial progress in molecular studies of pathogenic species such as *Candida albicans* and *Aspergillus fumigatus*, both of which evolved closely from the same phylogenetic lineage with the species of the model system listed above.

Since *C. neoformans* is a basidiomycetous fungus phylogenetically distant from model species such as *S. cerevisiae*, the research tools provided by the latter species offer more limited opportunities. Although the tools provided by *S. cerevisiae* made cloning and characterization of highly conserved genes or the genes responsible for synthesis of essential macromolecules for growth of *C. neoformans* possible, they were not directly useful for molecular study of virulence factors of the species. The plant pathogenic species of *Ustilago* which is phylogenetically closer to *C. neoformans* than *S. cerevisiae* is to *C. neoformans* may prove to be a more useful model system for molecular research in *Cryptococcus neoformans* than *S. cerevisiae*.

Cryptococcus neoformans is the only species of fungus with unarguable pathogenicity that has an extracellular polysaccharide capsule. The polysaccharide capsule is expressed only during the haploid stage (yeast) of its life cycle and has been identified as the major virulence factor in this pathogen. This is a genetically proven association of pathogenicity with the asexual life cycle in this species. Once two yeast cells of compatible mating type conjugate, the morphogenesis of the sexual state, *Filobasidiella neoformans*, begins with the formation of dikaryotic hyphal cells devoid of capsule. The basidia and basidiospores lacking capsule are formed at the end of the meiotic cycle. Another characteristic of *C. neoformans* believed to be associated with virulence of the species, melanin formation in the presence of diphenol oxidase substrates, is also expressed only during the asexual cycle.

Because *C. neoformans* is heterothallic, classical genetic analyses of these factors were carried out soon after its sexual life cycle was characterized in the late 1970's. Using the mutant strains of appropriate phenotypes, genetic studies on polysaccharide capsule formation (see cover photographs) and melanin production revealed their association with virulence. Molecular analysis of the virulence factors became possible with the development of a transformation system in haploid cells by 1990. The mutants created for classical analysis became an extremely useful tool, in fact the only available tool, for the cloning of virulence associated genes by complementation and molecularly prove their pathogenic role in the animal model. Molecular techniques such as differential cloning and complementation have been the two most powerful means used for the identification and characterization of the a mating type gene, also believed to be associated with virulence in *C. neoformans*. The molecular identification and exhaustive characterization of all virulence factors will eventually provide more *Cryptococcus*-specific drug targets. The molecular biological progress made in *Cryptococcus neoformans* over the past five years attests to the importance of collaborative research between medical and molecular researchers.

The question is how best to stimulate the application of this approach. Medical mycologists should examine the field of plant biology to see if there is a lesson to be learned. Plant biology advanced slowly until the mid-1980's; a major effort was made to promote research on the model organism *Arabidopsis*. Grants were specifically made to permit technology development and to train individuals in the care, handling, and manipulation of the organism. In the late 1970's, a similar approach, including excellent summer courses at Cold Spring Harbor, brought *S. cerevisiae* to its prominent position in biological research. It seems reasonable for the NIH to take a leadership role in this regard, much as the NSF and USDA took leadership roles in nurturing yeast and *Arabidopsis*.

Recommendations

- Fund technology development projects in industry and academia
- Organize industry workshops to disseminate technology
- Utilize BIONET
- Develop a stock center to store strains
- Have an annual molecular medical mycology meeting (the *Candida* meetings are now very good and of great value - perhaps they could be expanded)

- Encourage collaborative research between the medical and molecular researchers
- Make sure that the community knows about all the support services that are available (e.g., animal models for disease, stock centers, etc.)

SECRETION

Current Status

Extracellular factors are implicated in the pathophysiology of some medically important fungal infections. These include proteolytic, lipolytic and glycolytic enzymes, cell surface receptor and adhesion molecules, cell wall and capsular components, and products which modulate host immune responses. The post-synthetic transport of these factors through exocytic secretory pathways is a fundamental, but poorly understood, biologic process in fungi. Protein transportation and secretion pathways are comprised of three functionally integrated components.

Vesicular transport mechanisms direct vesicles containing post-synthetic proteins from the endoplasmic reticulum to the Golgi apparatus, vacuoles, plasmalemma and plasma membranes. Specific targeting, docking and fusion of vesicles with specific destination membranes (Golgi, vacuole or plasma membrane) is mediated by specific families of membrane proteins. These include GTP binding proteins, vesicle associated membrane proteins, syntaxins, vesicle fusion proteins, and attachment proteins and their receptors. These mechanisms have been described in considerable detail in the yeast *S. cerevisiae*. Recent studies indicate that transport/secretion mechanisms and their specific components are conserved in mammals and *Saccharomyces*. A second component directs the traffic of specific constituents within the vesicle transport pathway by regulating protein delivery to, and retention within, appropriate membrane compartments, or by directing the export of factors outside the plasma membrane, to either the cell wall or the environment. These events are mediated in part by specific targeting signals which are well characterized in *Saccharomyces*, but are only partially described in medically important fungi. These include secretion signal peptide sequences and vacuolar targeting signals within *N*-terminal pre- pro- peptides, and peroxisome-targeting sequences in the *C*-terminal amino acids of some proteins. Post-translational glycosylation and deglycosylation steps have also been shown to regulate the distribution and secretion of selected enzymes in some fungi.

The third component consists of enzymatic systems for processing proteins and glycoproteins within the vesicle transport network. Cleavage of pre- and pro- sequences of proteins and zymogens, glycosylation and deglycosylation, and enzyme activation events must occur in regulated sequences for appropriate and successful transport and export of functional products and factors. Although the system is well described in *Saccharomyces*, there is minimal knowledge of the enzymatic constituents responsible for protein processing in the medically important fungi.

Protein transportation and secretion pathways contribute indirectly to the overall zoopathogenic potential of fungi. These pathways have been elegantly dissected in *S. cerevisiae*. However, difficulties in performing molecular biology studies on medically important fungi has significantly hindered investigations. Our understanding of secretion in the latter organisms is highly fragmented and woefully incomplete. Delineation of vesicle-associated membrane proteins, syntaxins, attachment proteins and their receptors has not been accomplished in the medically important fungi. Secretion signal peptide sequences, targeting peptide sequences and glycosylation events have been characterized in only a few fungi, and mostly in non-medically important species. Protein-processing machinery in the pathogenic fungi is largely unexplored.

Our understanding of fungal mechanisms for the biosynthesis and assembly of cell walls, capsules, and cell surface receptors is rudimentary. The mechanism by which secretion products

enter, transit, and exit the cell wall is unknown. How factors and receptors are retained on the cell wall surface is unexplained. The related phenomenon of assimilation or endocytosis of extracellular material into fungal cells is also poorly understood, yet is highly germane to antifungal design and drug delivery strategies.

There are limited model systems for appropriately assessing the role of secreted products in the pathogenesis of medically important fungal infections. The apparent multifactorial nature of fungal virulence and the intrinsic redundancy of some fungal systems may confound the interpretation of gene knockout strategies that assess secreted virulence factors. However, successful models of pathogenic fungal infections in plants have elucidated the roles of secreted enzymes (cutinase, pisatin demethylase) and toxins (HC-toxin). The pathophysiology of phytofungal infection models may provide useful analogies for studying medically important fungal infections at both a biochemical and mechanistic level.

Despite the paucity of information on fungal secretion mechanisms, the field appears primed for study. The apparent conservation of transportation/secretion mechanisms in diverse species suggests that available technology and methodology may be successfully transferred from *S. cerevisiae* systems to some of the medically important fungi. Appropriate genetic and molecular biology systems need to be established in most cases, but may already exist in some species. Development of vacuolar protein sorting and secretion mutants in medically important yeasts and filamentous fungi may further elucidate the similarities and possibly differences in the secretion mechanisms of these organisms.

Although the conservation of secretion processes in eukaryotes suggests there will be many similarities with mammalism secretion systems, disparities might exist which could be exploited as targets for therapeutic drugs. Of particular interest are mechanisms for protein transportation across cell walls, a feature which distinguishes fungal pathogens from their mammalian hosts. Furthermore, participation of secretion pathways in the biosynthesis of cell walls may also provide relevant targets for antifungal agents. Fungal mechanisms of endocytosis may provide equally important targets.

Recommendations

- Interactions between plant pathologists and medical mycologists were seen to be mutually beneficial. At the current time, workshops using a similar approach to the Medical Mycology workshop seem to be the appropriate means to facilitate such communication.

- It is important that the methods that have been developed in *Saccharomyces* be extended to filamentous fungi and in particular to human pathogenic systems. Use of gene knockouts in these systems could be particularly important. For example, can gene knockouts in fungi influence virulence?

- A forward genetic approach could also be useful for the identification of virulence genes. Hypo- or hypervirulent mutants could be isolated and the genes mapped, cloned and analyzed.

- A summer course to train mycologists in classical and molecular techniques would be used in this regard. Such a course could be based on the model of courses at Woods Hole.

- A serious concern was based on the extensive degree of conservation of secretion in all eukaryotes. This conservation could cause significant problems in drug development. Identification of mechanisms that are unique to the fungi will be important for drug

development. Possible unique properties might be secretion through the cell wall, secretion of toxins, and unique fungal antigen processing.

- The study of endocytosis was considered to be at least as important as secretion for the development of antifungals. The isolation of endocytosis mutants in pathogenic fungi could therefore be an important approach.

- Secretion is an area for which there is extensive research in both academic and industrial settings. Communication between researchers in these areas is critical as well as communication between clinical and laboratory medical mycologists and between mycologists and genetic or molecular biologists.

CELL SURFACE AND SIGNALING SESSION

Current Status

Attachment and adherence of microorganisms to host cells has been studied extensively. With *Candida*, at least four recognition systems have been described, each based upon the nature of the *Candida* adhesin (mannoprotein or mannan), the type of host cell (epithelial, endothelial, or platelet), and the type of host cell ligand (glycoside or protein). The System I adhesin of the organism is a mannoprotein lectin which recognizes fucosyl or glucosamine glycosides of epithelial cells. The System II adhesin resembles functionally the "integrin" receptors of mammalian cells. It is a mannoprotein also but recognizes protein (RGD) ligands of platelets, endothelial cells, or the RGD domains of extracellular matrix proteins of endothelial cells. A System III adhesin (mannan) has been described which promotes the adherence of the organism to epithelial cells: however, this adhesin clearly differs from the the System I adhesin which is a mannoprotein and utilizes the protein component to recognize the ligand. More recently, a System IV adhesin (mannoprotein) has been described which seems to be associated with the colonization of splenic tissue by the organism.

Most of the observations in regard to adhesins as virulence factors is correlative, i.e., strains less adherent *in vitro* are also less virulent. These strains are often constructed by mutagenesis and are only presumed to be isogenic to the wild type in regard to all phenotypic properties except adhesins.

Two other medically important organisms under study to define systems of recognition, are *Cryptococcus neoformans* and *Aspergillus fumigatus*. The interplay between the recognition of *Cryptococcus* by phagocytes via interaction with immunoglobulin, the complement component C3, the capsular polysaccharide, and yeast cell receptors for the polysaccharide has been described by a number of workers. In addition, information is now appearing on how the recognition and signalling associated with mating in *Cryptococcus* occurs. Finally, in studies with *Aspergillus*, recognition of fibronectin via specific receptors has been described, as well as the interaction between conidia and C3. In all of these systems, however, the work to date has been focused on the cell surface and the role it plays in recognition. Little has been done to explore the next step in which the recognition act results in signal transduction. Likewise, little has been done to examine cell signalling in any other context in medically important fungi.

In basic mycology, much more is known about the cell surface, beginning with the synthesis of the cell wall. The interplay between the three described chitin synthases that occurs in cell growth and budding has been determined for *Saccharomyces*. Studies in *Candida albicans* suggest that analogous systems control the deposition of chitin in the cell wall of this medically important fungus. Although the processes involved in crosslinking the cell wall material are unknown, the

promise chitin holds as a fungal-specific drug target suggests that the area will continue to be a fertile one for research.

The process of cell recognition in mating (the pheromone response) and the subsequent cell signalling which occurs has been studied in considerable depth in *Saccharomyces cerevisiae*. With *Saccharomyces*, cells of the opposite mating types, designated a- and a- cells, fuse as an initial step in the mating process. Fusion is promoted by the a- and a- sexual agglutinins, mannoproteins found on the surface of a- and a- cells, respectively. The genes encoding these agglutinins have been cloned and sequenced, processing of the mannoproteins studied, and the signal transduction pathways elucidated. The similarity in structure of the a-agglutinin to the folded V region of the immunoglobulin family opens interesting questions concerning similarities in cell recognition/ signalling among eukaryotes, which may contribute to our understanding of how pathogens, such as *Candida* recognize host cells. Finally, in plant pathology, conidial attachment to potential host tissues through lectin-carbohydrate interactions has been characterized in numerous systems. Little advantage has been taken of this data by medical mycologists in examining potentially similar systems.

Recommendations

- Analogies between the *Candida* mannoprotein adhesins and the mannoprotein agglutinins of *S. cerevisiae* may justify collaborative efforts between these two groups of scientists in regard to gene isolation, signal transduction, and the study of trafficking and processing of adhesin mannoproteins.

- The finding of the integrin type of receptors in both *Candida* and *Aspergillus* may imply a unanimity among pathogens in regard to host cell recognition. Again, investigators of both organisms might begin collaborative studies to search for common targets among pathogenic fungi.

- Cell signalling may be breached in the medically important fungi by modelling studies on sexual interactions in basic systems such as *Saccharomyces*. The potential for drug targeting, should an unusual signalling pathway be described in fungi, certainly exists.

- There was consensus that studies of cell wall synthesis were most likely to result in potentially useful antifungal agents.

- Translocation of molecules to the cell wall and their integration in the cell wall provide potential for drug targeting.

- Attachment is the first step in pathogenesis, and therefore is a prime process for strategies in vaccine development.

- Adhesin gene isolation, sequencing and disruption should contribute to an understanding of fungal pathogenesis and may lead to drug and vaccine development strategies.

- Collaborations should be developed between medical mycologists and plant pathologists working in this general area.

SUMMARY OF THE FUNGAL GENOME SESSION

Current Status

The characterization and understanding of the genome of medically important fungi are of essential importance if further progress is to be made into the pathobiology of these emerging opportunists. The study of genomic structures of pathogenic fungi is in its infancy. There are many questions about genomic organization such as karyotypic variation, physical and genetic maps, repetitive elements, and presence of extrachromosomal DNA which remain unanswered. Early studies on the pathogenic fungi suggest a karyotypic flexibility which may provide a source of genetic variability important in their ability to adapt to the host environment and cause disease. This variability may be due to new recombination mechanisms or to new adaptations of old ones.

Consistent with its position as the most common fungal pathogen, *Candida albicans* has been the most intensively studied. Progress on the genomic organization of this diploid fungus includes karyotype analysis, and partial genetic, physical, and macrorestriciton maps of the genome. There has also been some progress in understanding the association between phenotypic variation in *C. albicans* and chromosomal translocation. Preliminary evidence also suggests that these translocations may occur at sites of repeated DNA.

It is clear from early studies of the pathogenic fungal genomes that these structures have a certain plasticity which requires understanding. Therefore, it is essential that investigators learn from the work in the yeast model system of *Saccharomyces cerevisiae*. For instance, the elegant work combining genetics and molecular biology on the study of replication sites within the third chromosome of *S. cerevisiae* allows investigators to form certain hypothesis regarding replication in pathogenic fungi. Although it is uncertain whether pathogenic fungi have similar mechanisms, these model systems are essential for investigators to even begin to frame their questions regarding mechanisms. Collaboration between the model system molecular biologists and those studying pathogenic fungi will be necessary to expand our knowledge base rapidly in molecular biology of medically important fungi.

Expansion of work from the model systems into genomic structure of fungal pathogens has already begun. For example, telomeres are specialized structures at the ends of eukaryotic chromosomes. There have been detailed analyses of telomere sequence structure from a variety of fungal pathogens, including *C. albicans*, *T. glabrata*, *C. neoformans*, and *H. capsulatum*. In the comparison between species, there are conserved principles such as G-rich tandem short repeats running 5' to 3' towards the ends of chromosomes. However, there are differences in both length and specific sequence among these species. Also, there appear to be active mechanisms for adding telomeric sequences on broken DNA. These mechanisms have already had practical consequences for transformation studies. They may also represent mechanisms important in the ability of the organisms to change karyotypic structures.

Recommendations

- Emphasis on identification of certain prototype strains of each species which would be made available to all investigators at a certain site such as Fungal Genetic Stock Culture Center. A repository for vectors and libraries for each fungal pathogen, so that investigators in peripheral fields will need little background work to test their hypothesis.

- Encouragement of continued basic studies on genome structures such as ARSs, plasmids, transformation systems, gene disruptions, and physical mapping.

- Development of collaborations between model system molecular biologists and medical mycologists.

- Courting of bacterial/viral molecular biologists who study microbial pathogenesis into mycotic field.

- Widespread dissemination of information about the low level of biohazard posed by fungal pathogens (with a few exceptions) to laboratory workers.

- Emphasis on the fact that genomic structure studies have implications for directed drug-target development and are not simply an exercise in study of biological mechanisms. Hence the complexity and plasticity of the genome of fungal pathogens must be examined and understood.

- Cooperation between those using the pathogenic fungal genomes for epidemiology, diagnostic, and drug targets and those studying the molecular biology is vital.

TOPIC SUMMARY AND SPEAKERS

Morphogenesis

Chairperson: George Kobayashi, Ph.D., Washington University, St. Louis, MO

Theme Presentation: Garry Cole, Ph.D., University of Texas, Austin, TX

Research Presentations:
Carlos Gimeno, M.S., Whitehead Institute, Cambridge, MA
William Timberlake, Ph.D., MycoPharmaceuticals, Cambridge, MA
David Soll, Ph.D., University of Iowa, Iowa City, IA

Sexual and Asexual Cycles

Chairperson: William Timberlake, Ph.D., MycoPharmaceuticals, Cambridge, MA

Theme Presentation: June Kwon-Chung, Ph.D., NIH/NIAID, Bethesda, MD

Research Presentations:
Amar Klar, Ph.D., NIH/NCI, Frederick, MD
Aaron Mitchell, Ph.D., Columbia University, New York, NY

Secretion

Chairperson: Janet Kurjan, Ph.D., University of Vermont, Burlington, VT

Theme Presentation: Thomas Ray, M.D., University of Iowa, Iowa City, IA

Research Presentation: Olin Yoder, Ph.D., Cornell University, Ithaca, NY

Cell Surface/Signalling

Chairperson: Judith Rhodes, Ph.D., University of Cincinnati, Cincinnati, OH

Theme Presentation: Richard Calderone, Ph.D., Georgetown University, Washington, DC

Research Presentations:
Janet Kurjan, Ph.D., University of Vermont, Burlington, VT
Phillips Robbins, Ph.D., Massachusetts Institute of Technology, Cambridge, MA

Fungal Genome Structure

Chairperson: John Perfect, M.D., Duke University, Durham, NC

Theme Presentation: Paul T. Magee, Ph.D., University of Minnesota, Minneapolis, MN

Research Presentations:
Carol Newlon, Ph.D., New Jersey Medical School, Newark, NJ
Mike McEachern, Ph.D., University of California, San Francisco, CA

Poster Session

NIH Informational Session:
Dennis M. Dixon, Ph.D., NIH/NIAID/DMID
Peter Jackson, Ph.D., NIH/NIAID/DEA

Facilitators

- Joan Bennett, Ph.D., Tulane University, New Orleans, LA
- Myra Kurtz, Ph.D., Merck & Company, Rahway, NJ
- Ian Ross, Ph.D., University of California, Santa Barbara, CA
- Claude Selitrennikoff, Ph.D., University of Colorado, Denver, CO
- Jeffrey Edman, M.D., University of California, San Francisco, CA
- John Edwards, M.D., University of California at Los Angeles-Harbor Medical Center, Torrance, CA
- William Goldman, Ph.D., Washington University, St. Louis, MO
- Dexter Howard, Ph.D., University of California at Los Angeles, Los Angeles, CA
- Thomas Mitchell, Ph.D. Duke University, Durham, NC
- Brian Wong, M.D., University of Cincinnati, Cincinnati, OH
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